PTOL-413A (12-08)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Applicant Initiated Interview Request Form

Application No.: 10/559,407 First Named Applicant: KU, Yun-Hee

Examiner: STOCK Jr, Gordon J. Art Unit: 2877 Status of Application: second O/A after final

Tentative Participants:

(1) STOCK Jr, Gordon J. (2) Peter T. Kwon

(3) _____ (4) _____

Proposed Date of Interview: 01/07/2009 **Proposed Time:** 09:30 AM **AM/PM**

Type of Interview Requested:

(1) ☑ **Telephonic** (2) ☐ **Personal** (3) ☐ **Video Conference**

Exhibit To Be Shown or Demonstrated: ☐ **YES** ☑ **NO**

If yes, provide brief description: _____

Issues To Be Discussed

Issues (Rej., Obj., etc)	Claims/ Fig. #s	Prior Art	Discussed	Agreed	Not Agreed
(1) 112- 1st	1~10		☐	☐	☐
(2) 112-2nd	5 & 8		☐	☐	☐
(3)			☐	☐	☐
(4)			☐	☐	☐

☐ Continuation Sheet Attached

Brief Description of Argument to be Presented:

Refer to the Remark in the Supplementary Response.

An interview was conducted on the above-identified application on _____ .

NOTE: This form should be completed by applicant and submitted to the examiner in advance of the interview (see MPEP § 713.01).

This application will not be delayed from issue because of applicant's failure to submit a written record of this interview. Therefore, applicant is advised to file a statement of the substance of this interview (37 CFR 1.133(b)) as soon as possible.

Peter Kwon
Applicant/Applicant's Representative Signature

Peter T. Kwon
Typed/Printed Name of Applicant or Representative

45,300
Registration Number, if applicable

/Gordon Stock Jr/
Examiner/SPE Signature

Brief Description of Argument to be presented for Interview:

(Referring to the supplementary Response)

(1) Describe the over all process (briefly) of the blood testing.
See the Flow Chat on Page 14

(2) Discuss the amended claims 1, 5, and 8.
See pages 4~6

(3) Regarding the calculations of shearing stress (variations) as time function.
Relationships between the viscosity, resistance and pressure variation.
Background of the empirical equations
Pages 9~11.

(4) Describe the pre-calculated data.
Page 11, lines 12~15 & page 9 lines 8~10 and Fig.6

(5) Describe the consistent preset conditions:
Page 11, lines 21~24

(6) CCD Sensor Array
Page 12, lines 4~9

(7) Find the unknown pressure by using the graph;
Page 13, line 3~10

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Facsimile Cover

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Art Unit: 2877
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Total pages (cover included): 16

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Remark:

With respect to the Patent Application Serial No. 10/559407 (filing date:12/05/2005), the please find a copy of supplementary RESPNSE.. The applicant has already submitted a supplementary RESPNSE to the Central Fax Center system on 01/15/2009.

Please, review the supplementary response and re-consider the allowance for this instant invention.

Please, appoint an interview date (01/07/2009 Wed) and confirm the date through e-mail. Seoul time is 14 hours advance than the Eastern Time. Therefore, I will call you at 9:30~10:00 AM Eastern Time on the confirmed appoint date (Is this date 01/07/2009 Wed 9:30~10:00 AM good for you?)

Please, answer me through e-mail (taijunkwon@yahoo.com). Thank you.

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being facsimile transmission to the United States Patent and Trademark Office, Fax No. (571) 273-2431 on 01/05/2009 (Date)

Typed or printed name of person signing this certificate:

Peter T. Kwon

Signature: *Peter Kwon*

GWiPS

Global Wide International Patent Service Attorney Docket No. P5102/JRIM

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	KU, Yun-Hee
Serial Number:	10/559,407
Filed:	12/05/2005
For:	Apparatus for Measuring Blood Cell Deformability
Art Unit:	2877
Examiner:	STOCK Jr, Gordon J.
Confirmation No.:	5617

Supplementary Response

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the (third) Office Action of October 15, 2008, please amend the above-identified application as follows: (Please, discard the previously submitted Response on the date of 01/03/2009 and replace this Supplementary Response.)

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being facsimile transmission to the United States Patent and Trademark Office, Fax No. (571) 273-8300 on 01/05/2009 (Date).

Typed or printed name of person signing this certificate:

Signature: Peter Kwon Peter T. Kwon

SPECIFICATION AMENDMENT

Paragraph from Page 4, lines 6 to 8 is revised and replaced as below:

The disposable blood test kit (20) is made of a transparent material such as silicon, silica, quartz, glass, a polymer [[workable]] produced by a laser, an extruded polymer or ceramics.

Paragraph from Page 7, lines 3 to 8 is revised and replaced as below:

a screen (31) for projecting the diffracted images of the blood cells, which were generated by light [[scattering]] diffracting of blood cells passing through the slit channel; an image capturing unit (35) for capturing the images; a control unit (36) for determining the blood cell deformability and the shearing force on time based data of the captured images and measured pressure through the computer image analysis.

Paragraph from Page 7, lines 11 to 14 is revised and replaced as below:

The diluted blood sample is injected into the tiny blood sample pot (21) of the disposable blood test kit (20). When the blood sample penetrates through the slit channel and passes underneath the light emitting unit (10), the emitted light is [[scattered and]] diffracted through the deformed blood cells to project the images on the screen.

Paragraph from Page 8, lines 22 to 24 is revised and replaced as below:

At this point, the image capturing unit (35) enables capturing the deformed blood cell diffraction image projected on the screen while the blood sample is passed under the light emitting unit through the slit channel (22). For capturing the images, the image capturing unit (35), can be adopted either a CCD camera, digital camera, web camera, or a video camera[[, which are capable to capture thirty-three frames per second]].

Alternatively, the deformed blood cell diffraction image can be directly captured without projecting on the screen by adopting a CCD sensor array as the image-capturing unit (35). The CCD sensor array is able to detect the light intensity of the diffracted images and determine the [[iso-intensity curve of]] blood cell deformation from the detected light signal on the sensor array. Thus, the deformability can be determined from the diffracted light, which is directly projected on the CCD-sensor array without projecting screen.

Paragraph from Page 14, lines 18 to 20 is revised and replaced as below:

The slit channel (22) having a rectangular shape of height H, width W and length L is loaded with the operating pressures and fluid volume on both ends, and the shear rate could be calculated with the pre-calculated data of the volume variation from Equation 5 as follows:

Paragraph from Page 15, lines 6 to 9 is revised and replaced as below:

Because the volume of the blood sample is very small in the buffer solution, the effect of viscosity of the blood in the diluted blood sample may be ignored. Therefore, the viscosity of the diluted blood sample is considered the same as that of the buffer solution. Even [[tough]] though a different blood sample is diluted into the buffer solution, the viscosity of the diluted blood sample is negligibly changed.

Paragraph from Page 15, lines 18 to 22 is revised and replaced as below:

As an implementing example, it is a special character of the present invention that the shear stress can be obtained by the pre-measured data or pre-calculated data of the differential pressure without detecting the instant pressure. It is also possible to plot the graph of the blood cell deformability with respect to the shear force as a function of the time based on the pre-calculated shear stress.

CLAIM AMENDMENT

What is claimed is:

1. (currently amended) An instrument for measuring blood cell deformability comprising:

a disposable blood test kit (20) for directly containing blood sample,

a light emitting unit (10) disposed above said disposable blood test kit (20),

a measurement unit (30) for measuring the blood cell deformability,

said disposable blood test kit (20) comprises a blood sample pot (21) for containing the blood sample, a slit channel (22) for flowing the blood sample by a pressure difference, and a waste blood pot (23) for collecting the tested blood sample,

said measurement unit (30) comprises a differential pressure generator (33), which is connected to the disposable blood test kit (20) through a connecting tube and a valve (32) for generating the pressure difference between the blood sample pot (21) and waste blood pot (23), a pressure gauge (34) connected to the differential pressure generator (33) and the disposable blood test kit (20) for measuring the pressure difference, a [[screen (31)]] means for projecting diffracted images of the blood cell, an image capturing unit (35) for capturing the diffracted images, a control unit (36) for calculating the blood cell deformability[[,]] and variation of a shearing force[[, and]] according to the blood cell deformation on time based data received from the pressure gauge (34) and the image capturing unit (35), an output unit (37) for printing the calculated information on a sheet or displaying on an LCD screen, and a memory unit (38) for storing the calculated information and images,

[[wherein said control unit (36) calculates the blood cell deformability and shearing force as a function of time according to pre-calculated data, which are calculated and stored by a computer analyses on time based data of the captured image and pressure measurement, with or without applying instantly measured pressure data, and the diffracted images of the blood cells captured by the image-capturing unit (35) are analyzed by ellipse curve-fitting

computer software to determine the length (L) and width (W) of the analyzed elliptic images, and calculating the Deformation Index (DI) for determining the blood cell deformability and shearing force as a function of time]]

wherein said control unit (36) further calculates a shearing stress (τ) as a function of time, which is calculated and stored by a computer analyses based on time data of pressure measurements, alternatively, said shearing stress (τ) can be determined according to pre-calculated data of pressure without applying the instantly measured pressure data, and the diffracted images of the blood cells captured by the image-capturing unit (35) are analyzed by ellipse curve-fitting computer software to determine a length (L) and a width (W) of analyzed elliptic images, and calculates a Deformation Index (DI) for determining the blood cell deformability and the shearing stress (τ) as a function of time.

2. (previously amended) An instrument for measuring blood cell deformability as claimed in claim 1, wherein said differential pressure generator (33) is connected to the waste blood pot (23) of the disposable blood test kit (20) through a connecting tube and a valve (32) for generating vacuum pressure, negative pressure, at the waste blood pot (23), so that the blood sample flows toward the waste blood pot (23) through the slit channel (22).

3. (previously amended) An instrument for measuring blood cell deformability as claimed in claim 1, wherein said differential pressure generator (33-1) is connected to the blood sample pot (21) of the disposable blood test kit (20) through a connecting tube and a valve (32) for generating positive pressure at the blood sample pot (21), so that the blood sample flows toward the waste blood pot (23) through the slit channel (22).

4. (original) An instrument for measuring blood cell deformability as claimed in claim 1,

wherein said slit channel (22) is optically transparent and has a clearance with a rectangular shape.

5. (currently amended) An instrument for measuring blood cell deformability as claimed in claim 1, wherein said disposable blood test kit (20) is made of a transparent material, [[such as]] which is one of silicon, silica, quartz, glass, a polymer [[workable]] produced by a laser, an extruded polymer or ceramics.

6. (previously amended) An instrument for measuring blood cell deformability as claimed in claim 1, further comprises a heat control device, which is a thermo-electric component, a temperature control block, a hot-cold water jacket, or a halogen-lamp for adjusting and maintaining constant testing temperature surrounding the disposable blood test kit.

7. (currently amended) An instrument for measuring blood cell deformability as claimed in claim 1, wherein said image capturing unit (35) enables capturing the diffracted images of the deformed blood cell projected on [[the]] a screen.

8. (currently amended) An instrument for measuring blood cell deformability as claimed in claim 1, wherein said image capturing unit (35) enables directly capturing the diffracted images of the deformed blood cell by employing a CCD sensor array without projecting on [[the]] a screen.

9. (previously amended) An instrument for measuring blood cell deformability as claimed in claim 1, wherein said image capturing unit (35) can be adopted either a CCD sensor array, CCD camera, digital camera, web camera or video camera for capturing images.

10. (original) An instrument for measuring blood cell deformability as claimed in claim 1, wherein said light-emitting unit (10) is adopted as either a Laser Diode or Light Emitting Diode (LED).

REMARKS

Please, discard the previously submitted Response on the date of 01/03/2009 and replace this Supplementary Response.

With respect to the Objections of the Specification and Claims:

Regarding the objected Specification, the objections are revised by changing back to the original words and phrases or removing the new matter. Regarding the objected Claims, the objections are revised. Therefore, the objections of the Specification and the Claims are obviated by the above Specification and Claim Amendments.

With respect to the claim rejections under 35 U.S.C. 112 – first and second Paragraphs:

The ground rejections of claims 1 to 10 under 35 U.S.C. 112, first paragraph and second paragraph are obviated by the above Specification and Claim Amendments.

The examiner indicates that the description of the present specification is not enough to convey the claimed subject matter of the instant invention for the skilled person in the relevant art.

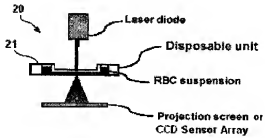
But, the inventor of the present invention asserts that the present specification has sufficiently described to carryout the claimed subject matter of the instant invention for the skilled person in the bio-medical art (blood testing technology).

However, the inventor will explain the instant invention in great detail for "measuring of the blood cell deformation, calculating the blood cell deformability, the variation of the shearing force (shear stress) according to the blood cell deformation based on time data received from the pressure gauge, and the images captured by the image capturing unit."

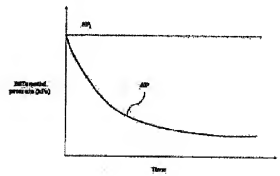
For better understanding, a process of the blood testing is presented as follows: a blood sample taken from a patient is diluted with the buffer solution to be a mixing ratio of

100:1 or 200:1 for testing.

(1) A blood test starts by placing a droplet of the diluted blood sample (0.5m*l*) in a blood sample pot (21) of a blood test kit (20) as shown a figure below.



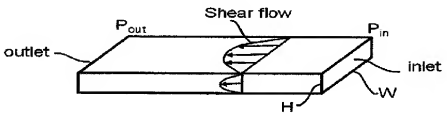
A switch is turned-on for operating a differential pressure generator (33) to generate a vacuum (negative) pressure in a slit channel (22). When the vacuum pressure applies to the waste blood pot (23), the blood sample will be penetrated into the slit channel (22). After completing the test, the blood sample is stored in the waste blood pot (23). The initial pressure difference (ΔP_i) is pre-set for operating. As the test progressing, the pressure variation is measured by the pressure gauge installed on the connecting tube between the waste blood pot (23) and the differential pressure generator (33). The operating vacuum pressure is exponentially varied as the pre-set initial pressure difference (ΔP_i) is approaching to the atmospheric pressure with the time elapse, $\Delta P(t) = (\Delta P_i) \exp(t)$, as shown in Fig. 6.



At this point, the blood cells in the diluted blood sample will be elongated as it flows through the slit channel due to the shearing force, which is caused by the resistance (friction)

against the walls of the slit channel (22).

Generally speaking, the flows of the diluted blood sample in the slit channel will be varied the velocities from the wall to the center of the tube, due to the resistance of the walls. This is a "shear flow," which is well known natural phenomenon of the fluid dynamics. As shown in the below figure, the shear flow is affected by the pressure difference (ΔP) of the inlet and the outlet, the viscosity of the fluid and the resistance of the wall.



The blood cells in the diluted blood sample would be elongated due to the shear forces in the slit channel (22). The shape and degree of the elongation of the blood cell are different depending on the patient's health condition, affected diseases, age and gender. This fact is also well known characteristics of the blood cell in the bio-medical technology.

In the office action, the examiner indicated that "*the applicant has not demonstrated what the relationship between the pressure (vacuum pressure) variation, the viscosity of the blood sample and the resistance of the slit channel to arrive at a calculated pressure using this pre-calculated data as consistent preset conditions.*"

With respect to the above questions, the present invention has adopted and applied the basic concepts, which are the shear flow of the natural phenomenon of the fluid dynamics, and the characteristics of the blood cell elongation in the shear flow, for utilizing to the blood testing.

Furthermore, it is not necessary to demonstrate the relationships between the affecting factors of the shear flow and the equations for calculating the deformation of the blood cell, because it has involved the numerous mathematical derivations and the plenty of the

experiments with simulations, which are outside scope of the instant invention.

However, the present specification has presented the empirical equations, which are the results of the mathematical derivations with the experiments, for calculating the blood cell deformability and shearing force.

A background of derivation of the empirical equation is briefly described as follows: regarding the viscosity of the blood sample, the viscosity of the blood is neglected because the blood sample is diluted with the buffer solution to be the mixing ratio of 100:1 or 200:1. The resistance (frictional factor) of the slit channel is determined through the simulations and experiments. Therefore, these factors of the viscosity and resistance are constant functions.

For simplifying the calculation, the affecting factors of the viscosity and the resistance are consistently pre-set as the non-variable functions for the empirical equation derivations. Through the numerous mathematical manipulation steps, the non-variable factors of viscosity and resistance are vanished in the empirical equations. Further, the pressure differential variation with time elapse, $\Delta P(t)$ can be pre-calculated or pre-determined with the experiment and the simulation. Then, the pre-calculated data of the pressure can be used instead of the instantly measured pressure data for calculating the shearing stress.

As the result, the empirical equations for calculating the blood cell deformability and shearing stress are introduced as a function of the pressure difference. Hereby, the empirical equations are presented for calculating the Deformability represented as a Deformation Index (DI) and the shear stress (τ) as shown in the instant Specification, pages 14 to 16.

Equation 1: $DI = (L-W)/(L+W)$ and Equation 6: $\tau = [\Delta P(t)\, H/L]/[(1+ 2H/W)]$.

Therefore, it is possible to input the consistent pre-set conditions, which are the initial pressure difference (ΔP_i), the viscosity of buffer solution and the resistance of slit channel, to the computer at a beginning of the blood testing by simply check-input a code number of the buffer solution and a model number of the test kit.

(3) The light emitting unit (10) emits the laser beams on the blood sample at the middle of slit channel (22) to project the images on the screen.

The examiner also indicated that *it is unclear how the image is captured "without projecting on the screen."*

The present invention employs a CCD sensor array to project the image instead of the conventional screen. The CCD sensor array has the multiple arrays (for example, 4 x 4), which forms a plurality of optical sensors in each array (for example, 2048 pixels). When the image is projected by the laser emitting unit, the projected image is captured by the optical sensors in the CCD sensor arrays to be interpreted and transformed to a digital signal for transmitting to the computer.

The deformation of the blood cell as the projected image is captured by the image capturing unit and analyzed by the ellipse curve-fitting computer software to measure a length (L) and a width (W) for calculating the deformability, which is represented by the Deformation Index (DI).

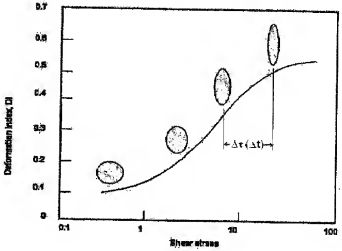
That is, the captured image is the actual blood cell deformation, and the calculated Deformation Index (DI) represents the deformability of the blood cell.

Once the Deformation Index (DI) and the shear stress (τ) are calculated through the computer programming, a graph is plotted with an ordinate as the Deformation Index (DI) (deformability) and an abscissa as the shearing stress, as shown figure below. The shearing stress (τ) is the function of the pressure variation with the time elapse.

The deformed blood cell has a tendency to resume the original shape (circular) with the time elapse as relief the shearing stress and the pressure difference. Thus, the deformed blood cell has a tendency to move from right to left along with the curve in the graph 7, i.e., the ellipse shaped blood cell tends to be the circular shaped blood cell as the time elapsed.

The smaller Deformation Index (DI) has the smaller deformability and the shape of

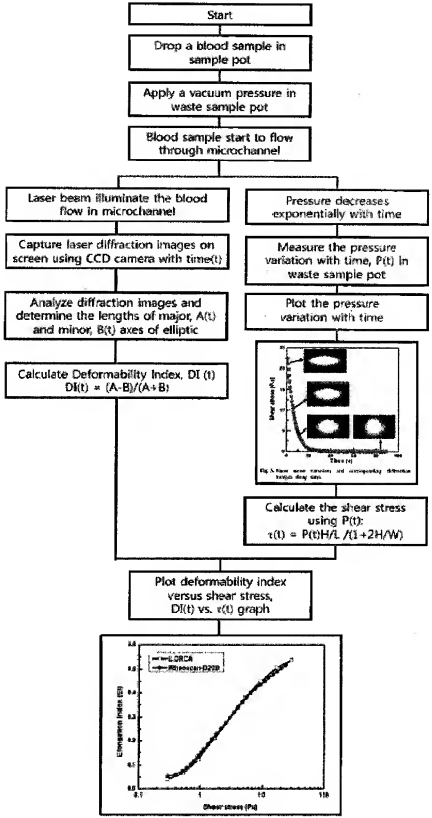
the blood cell tends to be closer to the circular shape, and vise versa. The larger shearing stress (τ) has the larger Deformation Index (DI) and the ellipse shape of the blood cell tends to be closer to the circular shape along with the curve of the Fig. 7, as the time elapsed.



Further, it is possible to calculate the unknown pressure variations with the known preset conditions and the pre-calculated data by reversely tracing the graphs.

For example, if a deformed shape of the blood cell with the known preset conditions is subject to identify, i.e., a code number of buffer solution (viscosity) and a model number of test kit (resistance) are known, but the pressure variation is not known, then the best matching deformed blood cell is searched via the ellipse curve-fitting computer software and read-in the shearing stress (τ) and the Deformation Index (DI) from the best matched graph, and the pressure variation is reversely calculated via the empirical equations.

(4) Hereinafter, a flow chart is presented to help easy understanding the process of the calculating deformability and shearing stress: a deformed image of the blood cell is captured by the image capturing unit (35) for calculating the deformability. The pressure difference (ΔP) is measured by the pressure gauge (34) for calculating the shear stress (τ) by the control unit (36). Then, a graph of the Deformation Index (DI) versus the Shear stress (τ) is plotted and displayed by the output unit (37).


Start
Drop a blood sample in sample pot
Apply a vacuum pressure in waste sample pot
Blood sample start to flow through microchannel
Laser beam illuminate the blood flow in microchannel
Capture laser diffraction images on screen using CCD camera with time(t)
Analyze diffraction images and determine the lengths of major, A(t) and minor, B(t) axes of elliptic
Calculate Deformability Index, DI (t)
DI(t) = (A-B)/(A+B)
Pressure decreases exponentially with time
Measure the pressure variation with time, P(t) in waste sample pot
Plot the pressure variation with time
Calculate the shear stress using P(t):
τ(t) = P(t)H/L /(1+2H/W)
Plot deformability index versus shear stress, DI(t) vs. τ(t) graph
Elongation Index (EI)
Shear stress (Pa)

14

Regarding a phrase of "according to pre-calculated data" (claim 1, line 20), the calculation of the shear force is distinctively divided to a shear stress (τ) as a function of the pressure variation (ΔP). Regarding the phrase of "such as" (claim 5, lines 2), it is revised to –which is one of–. A note is made that this phrase was revised to "such as," according to the paragraph 8 of the previous office action, mailed 03/13/2008. Regarding the rejected claim 8, a "screen" (claim 1, line 12) is revised to –means for projecting– to make claim 8 dependable to the independent claim 1.

Further, the examiner indicated that claims 1 to 10 would be allowable if rewritten to overcome the rejections. Thank you for indicating the allowable claims 1 to 10.

Accordingly, the objections of the Specification and Claims are amended to overcome the 35 U.S.C. 112 first paragraph and second paragraph rejections. The above amendments are supported by the current Specification. No New Matter is entered.

Hereby, the above additional description is sufficient to clearly understand the present invention.

Therefore, the applicant believes the present application is now in allowance condition and early Notice of Allowance is respectively solicited.

Respectfully submitted

Peter T. Kwon
Registration No. 45,300

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